Full Text AR-94-003

PROGRAM OF EXCELLENCE IN ORTHOPAEDIC BIOMATERIALS

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

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PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites investigators to submit interactive grant applications for a Program of Excellence in Orthopaedic Biomaterials. The several related projects should have a common theme or focus on a specific type of device or on an important research issue common to several types of devices. There should be a demonstrated positive interaction among the investigators and the projects. Individual projects may include basic, applied, or clinical research. The long range objective should be the development of improved and longer lasting orthopaedic devices.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Request for Applications (RFA), Program of Excellence in Orthopaedic

Biomaterials, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) awards.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) Interactive Research Project Grant (IRPG) mechanism. The IRPG mechanism encourages interaction and collaboration among scientists with common goals. It is intended to bring together research projects from investigators who wish to collaborate, but who do not require extensive shared resources. There should be constructive interchange of ideas, data, and/or materials. A minimum of two independent investigators are encouraged to submit concurrent, collaborative, cross-referenced individual research project grants (R01) or FIRST (R29) award applications. Applicants may be from one or several institutions. Detailed information about this mechanism of support is available in the NIH Program Announcement PA-93-078, NIH Guide for Grants and Contracts, Volume 22, Number 16, April 23, 1993. The total project period for applications submitted in response to the present RFA may not exceed four years for R01s.

Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicants. The anticipated award date is September 30, 1994. In addition to the requirements stated in this RFA, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50-000, revised October 1, 1991.

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to customary peer review procedures.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resources for conducting the proposed research. If so, a letter of agreement from either the GCRC program director or Principal Investigator could be included within the application.

FUNDS AVAILABLE

It is anticipated that the group of applications funded will result in one IRPG award made for a "Program of Excellence in Orthopaedic Biomaterials." The estimated funds available for the first year of support for this program are $700,000 in total costs. Actual funding is dependent on the receipt of a sufficient number of applications of high scientific merit. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years and the availability of funds.

This project is part of the NIH Advanced Material and Processing Program (AMPP) of the Federal Coordination Council for Science and Engineering Technology (FCCSET).

RESEARCH OBJECTIVES

Orthopaedic implants are commonly used in the treatment of musculoskeletal diseases and injuries. One major class of orthopaedic devices is used for fixation and includes pins, screws, wires, plates and rods. The other large class consists of joint replacement devices (e.g., total knee and total hip replacement systems). In 1992, there were an estimated 400,000 arthroplasties performed on knees or hips. Based on cross-sectional data gathered in 1988, it is estimated that approximately 5,000,000 people in the U.S. currently have an orthopaedic device implanted.

While these orthopaedic devices have had great general success in reducing the morbidity and disability that may result from musculoskeletal disorders, the long-term outcomes are not fully satisfactory; some devices require surgical replacement. As an example, failure of total hip devices may occur because of factors such as remodelling due to stress shielding, biological response to wear products, infection, other host/implant biological responses, or failure of any of the component devices or cement. Revision surgery is costly to perform and less likely to be successful than the original procedure. Public health cost savings could be greatly increased from orthopaedic devices that have an improved longevity.

The Program of Excellence in Orthopaedic Biomaterials will be a multidisciplinary effort combining advances in material and mechanical, science with recent progress in biological areas including immunology, molecular and cellular biology. The ultimate goal of this coordinated effort is fundamental, applied, or clinical knowledge that would lead to more effective long-term orthopaedic implants and improve the quality of life of the recipient patients.

The research investigators should have expertise in areas such as orthopaedic surgery, biomaterials, biomechanics, and biology. Each IRPG application should have a central theme or focus that serves to interconnect the component projects. There should be a demonstrated positive interaction among the investigators and the projects. Although clinical studies may be proposed, this RFA is not intended to support large clinical trials.

Appropriate research areas include, but are not limited to:

o Study of implant/host interface at molecular and cellular levels;

o Study of mechanisms of wear particle release from metals, ceramics, plastics, etc, and the host response to these particles in their natural and subsequent forms;

o Study of long-term response of bone to stress deprivation and develop approaches to minimize this effect;

o Investigation of underlying immune response to the large foreign body orthopaedic device;

o Investigation of origins and microcolonization of orthopaedic implants with infectious agents and optimal prevention and treatment of infections;

o Understanding of fundamental and clinical response to porous coatings and ingrowth enhancing coatings;

o Establishment of the potential role for stimulating bone growth into and around the implant with growth factors, angiogenic factors, and other modifiers of bone metabolism;

o Development of new biomaterials or innovative approaches to design or surgical implantation procedures;

o Establishment of innovative, accelerated procedures to assess the likely long-term response of biomaterials or devices;

o Exploration of production technologies and their influence on the final product that may lead to enhanced practical orthopaedic devices.

STUDY POPULATIONS

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including, but not limited to, clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

LETTER OF INTENT

Prospective applicants are asked to submit, by February 16, 1994, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIAMS staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Tommy Broadwater
Review Branch, Extramural Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 406
Bethesda, MD 20892
Telephone: (301) 594-9979

FAX: (301) 594-9673

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Information, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/435-0714; and from the NIH program administrator named below. Additional instructions for IRPG applications are in PA-93-038.

The RFA label available in the PHS 398 (rev. 9/91) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title (Program of Excellence in Orthopaedic Biomaterials) and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

Submit a signed, typewritten original of the applications, including the cover letter, checklist, and three signed, photocopies, in one package, whether or not the applications arise from the same institution, to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

Applications for the FIRST Award (R29) must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award (R29) applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

At the time of submission, two additional copies of the application must also be sent to:

Dr. Tommy Broadwater
Review Branch, Extramural Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 406

Bethesda, MD 20892
Telephone: (301) 594-9979
FAX: (301) 594-9673

Applications must be received by March 16, 1994. If an application is received after that date, it will be returned to the applicant without review. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by DRG and responsiveness by the NIAMS. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIAMS staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Applications may be triaged by an NIAMS peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official. Those applications judged to be competitive will undergo further scientific merit review. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific/technical merit by an appropriate peer review group convened by the NIAMS. The second level of review will be provided by the National Advisory Arthritis and Musculoskeletal and Skin Diseases Council.

Review criteria for RFAs are generally the same as those for unsolicited research grant applications:

o scientific, technical, or medical significance and originality of proposed research;

o appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;

o qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research;

o availability of the resources necessary to perform the research;

o appropriateness of the proposed budget and duration in relation to the proposed research.

The special value of the cooperative and interactive nature of the individual research applications and applicants comprising the IRPG should be emphasized in each application.

AWARD CRITERIA

The anticipated date of award is September 30, 1994.

Applications will compete for available funds with all other applications responsive to this RFA. The following items will be considered in making funding decisions:

o quality of the proposed program project grants as determined by peer review;
o availability of funds; and
o programmatic priorities.

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged.
The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Stephen L. Gordon
Musculoskeletal Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 407
Bethesda, MD 20892
Telephone: (301) 594-9951
FAX: (301) 594-9673

Direct inquiries regarding fiscal matters to:

Ms. Diane M. Watson
Grants Management Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 732A
Bethesda, MD 20892
Telephone: (301) 594-9955
FAX: (301) 594-9673

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal, and Skin Diseases. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78- 410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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